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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/508,849	03/17/00	NAGATA S	1110-266PCT

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EXAMINER	
HARRIS,A	

ART UNIT	PAPER NUMBER
1642	8

DATE MAILED: 05/22/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/508,849	Nagata And Tanaka
Examiner	**Art Unit**
Alana M. Harris, Ph. D.	1642

-- The MAILING DATE of this communication app ars on the cover sh t with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☐ Responsive to communication(s) filed on _____

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) 1-7 is/are pending in the applica

4a) Of the above, claim(s) _____ is/are withdrawn from considera

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) 1-7 is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirem

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☒ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☒ Certified copies of the priority documents have been received in Application No. 09/508,849 .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)

16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 4

18) ☐ Interview Summary (PTO-413) Paper No(s). _____

19) ☐ Notice of Informal Patent Application (PTO-152)

20) ☐ Other:

DETAILED ACTION

1. Claims 1-7 are pending.

Claims 1-7 are examined on the merits.

Priority

2. Acknowledgment is made of applicant's claim for foreign priority based on an application filed in Japan on September 17, 1997. It is noted, however, that applicant has not filed a certified copy of the Japanese application, Number 9-252541 as required by 35 U.S.C. 119(b). Hence, the effective filing date of the instant application is September 17, 1998 (PCT/JP98/04187).

Should applicant desire to obtain the benefit of foreign priority under 35 U.S.C. 119(a)-(d) prior to declaration of an interference, a translation of the foreign application should be submitted under 37 CFR 1.55 in reply to this action.

Specification

3. The disclosure is objected to because of the following informality: there are several misspelled words in the specification. Please note on page 6, line 4 the word, "effecter" and page 13, line 22 the word "stomac". The Applicants are requested to review the entire specification for similar errors and correct the listed errors, as well as any others.

Claim Objections

4. Claim 2 is objected to because it is not clear whether Applicants are referring to just one amino acid or both amino acids should be deleted or substituted when reading the recitation "...129th amino - 130th amino acid residues...".

Claim 3 is also objected to because it is not clear if just one or all sixty-one amino acid residues, corresponding to the recitation "...8th amino acid - 69th amino acid residues..." should be deleted or substituted.

Clarification is required.

Claim Rejections - 35 U.S.C. § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claim 1 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants claim a novel Fas ligand derivative which has protease resistance. This broad claim reads on all possible Fas ligand derivatives that are capable of being resistant to any and all proteases. Applicants are only in possession of Fas ligand derivatives identified as SEQ ID NO:1

and SEQ ID NO:2. Applicants are not in possession of all the vast number of derivatives that could be regarded as protease resistant. Many structurally unrelated amino acids are encompassed within the scope of these claims. The specification lacks information to lead one of skill in the art to understand that the applicant had possession of the broadly claimed invention at the time the instant application was filed.

Likewise, Applicant has not identified the protease to which the claimed invention is resistant. Applicants note on page 43 of the disclosure a protease that is likely to cleave a Fas ligand may belong to the ADAM family of proteases, specifically TNF-α -converting exzyme (TACE). However, this disclosure does not evidence that Applicant identified and was in possession of the claimed novel ligand that was resistant to this and only this protease out of a voluminous amount of proteases. Applicant was not in possession of the infinite number of Fas ligand derivitatives that could be possibly be produced by a number of proteases. Applicant is referred to the revised interim guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov. One skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

7. Claim 7 are rejected under 35 U.S.C. 112, first paragraph, because the specification, does not reasonably provide enablement commensurate with the scope of the claimed invention. The

specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Claim 7 is broadly drawn to "a method of preventing or treating a disease wherein Fas ligand-induced apoptosis is involved, wherein the Fas ligand derivative...or the apoptosis regulator...is administered." The specification does not disclose how to use the instant invention for the treatment of disease in any animal. The specification is enabled for the Fas ligand derivative *in vitro* treatment of hepatocytes as disclosed on page 28 of the specification, however the specification is not enabled for the *in vivo* treatment of any disease, wherein Fas ligand-induced apoptosis is involved. The state of the art is such that is unpredictable in the absence of in vivo data (as per the specification) as to whether the instant invention can be used for the treatment of human disease. Hurtenbach et al. (J. Exp. Medicine 177:1499-1504, 1993) teaches that peptide administration can provoke "severe immunological side effects" (see page 1503, second column). Hurtenbach et al. teach that peptides are currently unsuitable for therapeutic use (see page 2503, second column, last two lines).

Regarding the use of peptides for therapeutic purposes, pharmaceutical therapies in the absence of appropriate in vivo data establishing that said peptides can be used for the treatment of humans are unpredictable for the following reasons; (1) the peptide may be inactivated before producing an effect, i.e., proteolytic degradation, immunological inactivation or due to the inherently short half life of the peptide; (2) the peptide may not reach the target area because i.e. the protein may not be able to cross the mucosa or the protein may be absorbed by fluids, cells

and tissues where the protein has no effect; and (3) other functional properties, known or unknown, may make the peptide unsuitable for in vivo therapeutic use, i.e., such as an adverse side effects prohibitive to the use of such a treatment, See page 1338, footnote 7 of Ex parte Aggarwal, 23 USPQ2d 1334 (PTO Bd. Pat. App. And inter. 1992).

There is no guidance in the specification as to how to determine which peptide or combination of peptide derivatives can be administered to any particular individual for the treatment of a vast number of diseases involving Fas ligand-induced apoptosis. It appears that undue experimentation would be required of one skilled in the art to practice the instant claimed invention using the teachings of the specification. See Ex parte Forman, 230 USPQ 546 BPAI, 1986.

In absence of guidance and/or working examples, one skilled in the art would reasonably conclude that a large number of peptides could be made, however, the specification has not taught how all the molecules would be effective in preventing or treating the recited disease. The scope of the claims must bear a reasonable correlation with the scope of enablement. One skilled in the art would be forced into undue experimentation in order to practice the broadly claimed invention.

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 1-5 and 7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claims 1-5 and 7 are vague and indefinite in the recitation "derivative. It is not clear what possible peptide combinations and how many peptides are encompassed by the claimed "derivative". As written it is impossible for one skilled in the art to determine the metes and bounds of the claims.

b. Claim 6 is vauge and indefinite in the recitation "apoptosis regulator". What is regarded as an apoptosis regulator? Are a set of amino acids regarded as an apoptosis regulator only if a soluble Fas ligand is included? How does an apoptosis regulator function?

c. The recitation "...Fas ligand-induced apoptosis is involved" in claim 7 is vague and indefinite. What is meant by the term "involved"? In what manner is the Fas ligand-induced apoptosis involved? Accordingly, as the claim is written it is impossible for one skilled in the art to determine the metes and bounds of the claims.

Claim Rejections - 35 U.S.C. § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. Claims 1 and 5-7 are rejected under 35 U.S.C. 102(a) as being anticipated by WO 98/21232 (May 22, 1998/ referenced on IDS). The abstract and page 3, lines 6-16 of this document disclose SEQ ID NO:12, a novel Fas ligand derivitive which is non cleavable, hence protease resistant. This disclosed derivative is regarded as an apoptosis regulator including a soluble Fas ligand. SEQ ID NO:11 of the WO document is the DNA coding for the novel Fas ligand derivative of claim 1.

This document also discloses general methods of preventing or treating a disease wherein Fas ligand-induced appoptosis is involved. On pages 16-18 of the document methods are disclosed wherein the Fas ligand deriviative and the apoptosis regulaotor is administered.

12. Claims 2, 3, 5 and 6 are rejected under 35 U.S.C. 102(b) as being anticipated by Suda et al. (Cell 75:1169-1178, December 17, 1993), as evidenced by Accession 49266 (January 13, 1995). Suda discloses a novel Fas ligand derivative on page 1171, Figure 2 having an amino acid sequence of the natural human Fas ligand wherein the 129th amino acid residue from the N terminal is substituted and at least one of 111th amino acid-128th amino and the 131st and 133rd amino acid residue from the N terminal is substituted (also see attached database sheet).

Additionally, Suda discloses a novel Fas ligand derivative having an amino acid sequence of the natural human Fas ligand wherein several amino acids residues from the N terminal end

corresponding to the 8th - 69th amino acids are deleted and substituted, the 129th amino acid residue is substituted and at least one amino acid residue of the 111th amino acid- 128th amino acid residues or 131st and 133rd amino acid reside from the N terminal is substituted.

The DNA coding for the novel Fas ligand derivative is also disclosed in Figure 2 of the Suda reference. The disclosed amino acid sequences are intrinsically regarded as an apoptosis regulator including a soluble Fas ligand. The art of record is evidenced to be the same as that claimed since there is no evidence distinguishing the disclosed prior art from the claimed invention.

13. Claim 4 is free of the art.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alana M. Harris whose telephone number is (703) 306-5880. The examiner can normally be reached on Monday through Friday from 6:30 am to 4:00 pm, with alternate Fridays off. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached on (703) 308-3995. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Alana M. Harris, Ph.D.

Patent Examiner, Group 1642
May 16, 2001

SHEELA HUFF
PRIMARY EXAMINER